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<110> Lechler, Robert I.  
Dorling, Anthony

<120> IMMUNOSUPPRESSION BY BLOCKING T CELL CO-STIMULATION SIGNAL 2 (B7/CD28 INTERACTION)

<130> 2292/0H795

<140> US 09/674,462

<141> 2001-05-08

<150> PCT/ GB99/01350

<151> 1999-04-30

<160> 27

<170> PatentIn Ver. 2.1

<210> 1

<211> 223

<212> PRT

<213> Sus scrofa

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Ser Arg Thr Trp Pro Cys Thr Ala Leu Phe Ser Leu Leu Phe Ile Pro  
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Val Phe Ser Lys Gly Met His Val Ala Gln Pro Ala Val Val Leu Ala  
35 40 45

Asn Ser Arg Gly Val Ala Ser Phe Val Cys Glu Tyr Gly Ser Ala Gly  
50 55 60

Lys Ala Ala Glu Val Arg Val Thr Val Leu Arg Arg Ala Gly Ser Gln  
65 70 75 80

Met Thr Glu Val Cys Ala Ala Thr Tyr Thr Val Glu Asp Glu Leu Thr  
85 90 95

Phe Leu Asp Asp Ser Thr Cys Thr Gly Thr Ser Thr Glu Asn Lys Val  
100 105 110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Val Asp Thr Gly Leu Tyr Ile  
115 120 125

Cys Lys Val Glu Leu Leu Tyr Pro Pro Pro Tyr Tyr Val Gly Met Gly  
 130 135 140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser  
 145 150 155 160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe  
 165 170 175

Tyr Ser Phe Leu Ile Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys  
 180 185 190

Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu  
 195 200 205

Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn  
 210 215 220

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 <211> 672  
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 <213> Sus scrofa

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 gccaacctg cagtagtgct ggccaacagc cggggtgttg ccagctttgt gtgtgagtat 180  
 gggctctgag gcaaagctgc cgaggtccgg gtgacagtgc tgcggcgggc cggcagccag 240  
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 tctacatgca ctggcacctc caccgaaaac aaagtgaacc tcaccatcca agggctgaga 360  
 gccgtggaca ctgggctcta catctgcaag gtggagctcc tgtaccacc accctactat 420  
 gtgggtatgg gcaacgggac ccagatttat gtcattgac cagaaccatg cccagattct 480  
 gatttcctgc tctggatcct ggcagcagtt agttcagggt tgttttttta cagcttcctc 540  
 atcacagctg tttctttgag caaaatgcta aagaaaagaa gtcctcttac tacaggggtc 600  
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<210> 3  
 <211> 400  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> pCTLA4-Ig construct (Figure 4)

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 <211> 729  
 <212> DNA  
 <213> Phage library

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 gagactctcc tgtgcagcct ctggattcac ctttagcagc tatgccatga gctgggtccg 120  
 ccaggctcca ggaagggggc tggagtgggt ctcagctatt agtggtagtg gtggtagcac 180  
 atactacgca gactccgtga agggccgggt caccatctcc agagacaatt ccaagaacac 240  
 gctgtatctg caaatgaaca gcctgagagc cgaggacacg gccgtgtatt actgtgcaag 300  
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 tggaggcggg tcaggcggag gtggctctgg cggtagtgca cttcagctctg tgctgactca 420  
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 caagtctggc acctcagcct ccctggccat cagtgggctc cggtcaggag atgaggctga 660  
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 cctaggtgc 729

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 ccggcagccc ccagggaagg gactggagtg gattgggtat atctattaca gtgggagcac 180  
 caactacaac ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca 240  
 gttctccctg aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcaag 300  
 aatgcggaag gataagtttg actattgggg ccaaggtacc ctggtcaccg tctcgagtgg 360  
 tggaggcggg tcaggcggag gtggctctgg cggtagtgca cttcagctctg tgctgactca 420  
 gccaccctca gcgtctggga cccccgggca gagggtcacc atctcttggt ctggaagcag 480  
 ctccaacatc ggaagtaatt atgtatactg gtaccagcag ctcccaggaa cggcccccaa 540  
 actcctcatc tataggaata atcagcggcc ctcaggggtc cctgaccgat tctctggctc 600  
 caagtctggc acctcagcct ccctggccat cagtgggctc cggtcaggag atgaggctga 660  
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 cgtccctaggt gcggccgc 738

<210> 8  
 <211> 739  
 <212> DNA  
 <213> Phage library

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 caggcccctg gacaagggct tgagtggatg ggaataatca accctagtgg tggtagcaca 180

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caagctacgc acagaagttc cagggcagag tcaccatgac cagggacacg tccacgagca 240
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gaatggctcc ctatgtgaat acgcttgttt tttggggcca aggtaccctg gtcaccgtct 360
cgagtgggtg aggcggttca ggcggagggtg gctctggcgg tagtgactt cagtctgtgc 420
tgactcagga cctgctgtg tctgtggcct tgggacagac agtcaggatc acatgccaaag 480
taggagacag cctcagaagc tattatgcaa gctggtacca gcagaagcca ggacaggccc 540
ctgtacttgt catctatggt aaaaacaacc ggccctcagg gatcccagac cgattctctg 600
gctccagctc aggaacacac gcttccttga ccatcactgg ggctcaggcg gaagatgagg 660
ctgactatta ctgtaactcc cgggacagca gtggttttac tgtattcggc ggagggacca 720
agctgaccgt cctaggtgc                                     739

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<210> 9  
 <211> 729  
 <212> DNA  
 <213> Phage library

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gccagatgcc cgggaaaggc ctggagtgga tggggatcat ctatcctggg gactctgata 180
ccagatacag cccgtccttc caaggccagg tcaccatctc agccgacaag tccatcagca 240
ccgcctacct gcagtggagc agcctgaagg cctcggacac ggccgtgtat tactgtgcaa 300
gattttcgtc tgggtggttt gactattggg gccaaaggtag cctggtcacc gtctcagagt 360
gtggaggcgg ttcaggcgga ggtggctctg gcggtagtgc acttgacatc cagttgaccc 420
agtctccatg ttctgtctct catctgtagg agacagagtc accatcactt gccgggcccag 480
tcagggcatt agcagttatt tagcctggtg tcagcaaaaa ccagggaag cccctaagct 540
cctggtctat gctgcatcca ctttgcaaag tgggggtccc tcaagggtca gcggcagtg 600
atctgggaca gaattcactc tcacaatcag cagcctgcag cctgaagatt ttgcaactta 660
ttactgtcaa cagcttaata gttaccgctt gacgttcggc caagggacca agctggaaat 720
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<210> 10  
 <211> 240  
 <212> PRT  
 <213> Phage library

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
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Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
  35              40              45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
  50              55              60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

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Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn  
50 55 60

Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn  
65 70 75 80

Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val  
85 90 95

Tyr Tyr Cys Ala Arg Met Arg Lys Asp Lys Phe Asp Tyr Trp Gly Gln  
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly  
115 120 125

Gly Ser Gly Gly Ser Ala Leu Gln Ser Val Leu Thr Gln Pro Pro Ser  
130 135 140

Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser  
145 150 155 160

Ser Ser Asn Ile Gly Ser Asn Tyr Val Tyr Trp Tyr Gln Gln Leu Pro  
165 170 175

Gly Thr Ala Pro Lys Leu Leu Ile Tyr Arg Asn Asn Gln Arg Pro Ser  
180 185 190

Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser  
195 200 205

Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Val  
210 215 220

Ala Ala Trp Asp Asp Ser Leu Phe Val Phe Gly Gly Gly Thr Lys Leu  
225 230 235 240

Thr Val Leu Gly Ala Ala  
245

<210> 12  
<211> 242  
<212> PRT  
<213> Phage library

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1 5 10 15



<400> 13

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Ser	Leu	Lys	Ile	Ser	Cys	Lys	Gly	Ser	Gly	Tyr	Ser	Phe	Thr	Ser	Tyr
			20					25						30	
Trp	Ile	Gly	Trp	Val	Arg	Gln	Met	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Met
		35					40						45		
Gly	Ile	Ile	Tyr	Pro	Gly	Asp	Ser	Asp	Thr	Arg	Tyr	Ser	Pro	Ser	Phe
	50					55					60				
Gln	Gly	Gln	Val	Thr	Ile	Ser	Ala	Asp	Lys	Ser	Ile	Ser	Thr	Ala	Tyr
	65				70					75					80
Leu	Gln	Trp	Ser	Ser	Leu	Lys	Ala	Ser	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Phe	Ser	Leu	Gly	Gly	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu
			100					105					110		
Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly
		115					120					125			
Gly	Ser	Ala	Leu	Asp	Ile	Gln	Leu	Thr	Gln	Ser	Pro	Ser	Phe	Leu	Ser
	130					135					140				
Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly
	145				150					155					160
Ile	Ser	Ser	Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro
				165					170					175	
Lys	Leu	Leu	Val	Tyr	Ala	Ala	Ser	Thr	Leu	Gln	Ser	Gly	Val	Pro	Ser
			180					185					190		
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser
		195					200						205		
Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Leu	Asn
	210					215					220				
Ser	Tyr	Arg	Leu	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg
	225				230					235					240



Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly  
 130 135 140  
 Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser  
 145 150 155 160  
 Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe  
 165 170 175  
 Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys  
 180 185 190  
 Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu  
 195 200 205  
 Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn  
 210 215 220

<210> 16  
 <211> 773  
 <212> DNA  
 <213> Homo sapiens

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 ctggatcgga cctggaacct gggcgagaca gtggagctga agtgccaggt gctgctgtcc 180  
 aaccgcagct cgggctgctc gtggctcttc cagccgcgcg gcgccgccgc cagtcccacc 240  
 ttctctctat acctctccca aaacaagccc aaggcggccg aggggctgga caccagcgcg 300  
 ttctcgggca agaggttggg ggacaccttc gtcctcacc tgagcgactt ccgccgagag 360  
 aacgagggct actatttctg ctcggccctg agcaactcca tcatgtactt cagccacttc 420  
 gtgccggtct tectgccagc gaagcccacc acgacgccag cgccgcgacc accaacaccg 480  
 gcgccacca tcgcgtcgca gccctgtgct ctgcgcccag aggcgtgccg gccagcgggc 540  
 gggggcgagc tgcacacgag ggggctggac ttgcctgtg atatctacat ctgggcgccc 600  
 ttggccggga cttgtggggc ctttctctct tcaactgtta tcacccttta ctgcaaccac 660  
 aggaaccgaa gacgtgtttg caaatgtccc cggcctgtgg tcaaatacgg agacaagccc 720  
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 <213> Artificial Sequence

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<210> 18  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 18  
 taatgaattc tcaattgatg ggaataaaat aag 33

<210> 19  
 <211> 60  
 <212> DNA  
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<220>  
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<400> 19  
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<210> 20  
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 <212> DNA  
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<220>  
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<400> 21  
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<210> 22  
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<220>

<223> PCR primer

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<210> 23

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 23

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33

<210> 24

<211> 76

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

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<210> 25

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 25

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29

<210> 26

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

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33

<210> 27

<211> 73

<212> DNA

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<223> PCR primer

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